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EXAMINER	
SZPERKA, MICHAEL EDWARD	
ART UNIT	**PAPER NUMBER**
1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	10/663,215	SHERMAN ET AL.
	Examiner	Art Unit
	Michael Szperka	1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 May 2005 and 15 July 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-50* is/are pending in the application.

4a) Of the above claim(s) *17-29 and 42-50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *30-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

SDO

DETAILED ACTION

1. Applicant's response and amendments filed May 13, 2005 and July 15, 2005 are acknowledged.

Claims 1-16 have been cancelled.

Claims 19, 23, 25, 29, 30, 34, 36, 42, and 49 have been amended.

Claims 17-50 are pending in the instant application.

Applicant's election with traverse of Group IV, claims 30-41, drawn to peptides and compositions comprising peptides that elicit an antibody response specific for adherent erythrocytes in the reply filed on May 13, 2005, and the species election of SEQ ID NO:5 on July 15, 2005, is acknowledged. The traversal is on the ground that all groups can be searched without undue burden. This is not found persuasive because of the reasons of record set forth in the restriction requirement set forth in the office action mailed March 18, 2005.

The requirement is still deemed proper and is therefore made FINAL.

Claims 17-29 and 42-50 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions. Applicant timely traversed the restriction (election) requirement in the reply filed on May 13, 2005.

The elected species of SEQ ID NO:5, YETFSKLIKIFQDH, is a fragment of the erythrocyte band 3/anion exchage-1 protein, for which the full length sequence and

many specific peptide fragments are known in the prior art. However, none of the sequences disclosed in the prior art appear to be only the 14 amino acids of SEQ ID NO:5. As such, the art search has been extended beyond the elected species.

Claims 30-41 are under examination in the instant application.

Specification

2. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.
Line 2 of page 24 contains a link to the NCBI website that might be disabled due to the way in which it is disclosed. However, to ensure that the link is disabled, the examiner suggest amending the section to read "... (and can be found on the world wide web at ncbi.nlm.nih.gov)."

Claim Objections

3. Claims 34 and 40 are objected to because in their current form it is unclear if the claimed peptide, or composition comprising a peptide, is SEQ ID NO:5 itself, (i.e. a single 14 amino acid peptide of defined sequence) or if it is a peptide of between 14 and 40 amino acids that comprises the entire sequence of SEQ ID NO:5. Amending the claims to remove this ambiguity is suggested.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 30-41 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for peptides and compositions comprising SEQ ID NO:5 that induce an antibody response that can lead to the lysis of adherent red blood cells, does not reasonably provide enablement for peptides and compositions comprising SEQ ID NO:6 or polypeptides 80% identical to SEQ ID NO:6 that that induce an antibody response that directly lyses adherent red blood cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Applicant has claimed peptides, and compositions comprising peptides, wherein the peptide is no longer than 40 amino acids, comprises a sequence at least 80% identical to SEQ ID NO:6, wherein the undefined (X) residues of SEQ ID NO:6 bear a charge at physiological pH, and are capable of eliciting antibodies that lyse pathologically adherent erythrocytes. Applicant has disclosed the genus sequence of SEQ ID NO:6 and has provided a working example in Example 3 that immunization of rabbits with the peptide of SEQ ID NO:5 (a member of the genus of SEQ ID NO:6) elicits a polyclonal antibody response that is capable of lysing human erythrocytes infected with *P. falciparum*, but not uninfected erythrocytes, in the presence of serum

that contains active complement components (see particularly page 38 and Figures 6 and 7). As such, it is clear that the peptide of SEQ ID NO:5 contains all of the requisite structural and functional properties, but it does not appear that this can be said of all members of the genus of SEQ ID NO:6.

SEQ ID NO:6 is a generic sequence, Y X_1 TFS X_2 LI X_3 IFQ X_4 X_5, which contains five undefined residues. The recitation that the X residues bear a charge at physiological pH is not a meaningful limitation since all amino acids bear a charge at physiological pH due to the presence of $NH3^+$ and COO^- moieties present in the amino acid, but only amino acids that have a charged side chain bear a *net* charge at physiological pH. As such, X_1-X_5 can be any amino acid except when their identity is explicitly defined; such as in claim 33, which recites that X_2 and X_3 are lysine residues. Additionally, the claims recite that the claimed peptide is 40 or fewer amino acids comprising a sequence with at least 80% sequence identity to SEQ ID NO:6. However, the claims do not indicate that the claimed sequences need to be 80% identical to the entire length of SEQ ID NO:6. This means that peptides comprising 80% identical fragments of SEQ ID NO:6 are encompassed by the scope of the claims, with a reasonable size for a fragment being as small as two amino acids.

All of the claimed peptides (and compositions comprising said peptides) are recited as having the functional property of being able to elicit an antibody response that can lyse pathologically adherent erythrocytes. The phrase "pathologically adherent erythrocytes" is defined in paragraph 51 of page 15 of the specification as cells that display altered conformations of band 3/anion exchange-1 protein due to infection or

disease, wherein the altered conformations expose cryptic neoantigens. It should be noted that antibodies to band 3/anion exchange-1 protein will not lyse cells directly. Rather, as taught by Janeway et al., antibody binding to cells leads to the recruitment of C1q molecule and the initiation of the classical pathway of complement activation that results in lysis of the target cell (Immunobiology, third edition 1997, pages 8:2 and 8:34-8:37, see entire selection, particularly Figures 8.1, 8.32, and 8.36). As such, it is complement cascade, rather than the antibody itself, that lysis the cell. Therefore, applicant's recited functional limitation is not enabled as currently recited. Note that Applicant's working example in example 3 uses diluted rabbit antiserum, the antiserum being the source of both the antibodies and the complement in the experimental system.

Further, the claimed peptides and compositions must be capable of eliciting an antibody response wherein the antibodies bind to the wild type sequence of band 3/anion exchange-1 protein found in erythrocytes of infected or diseased patients. Colman (Research in Immunology, 1994, 145:33-36) teaches that even single amino acid changes in the antigen can completely disrupt the binding between an antibody and an antigen (see particularly the paragraph that starts in the right column of page 33). It is also known that people living in malaria infested areas make antibodies directed against loop 3 of the band 3/anion exchange-1 protein (i.e. the region where SEQ ID NO:5 and degenerate SEQ ID NO:6 are located in the full length protein) and that these autoantibodies are not involved in hemolysis (Hogh et al., Infection and Immunity, 1994, 62:4362-4366, see entire document, particularly the abstract). As

such, an antibody response elicited to some member of the genus of peptides comprising sequences 80% identical to SEQ ID NO:6 may not be able to bind to the wild type sequence of band 3/anion exchange-1 protein (i.e. SEQ ID NO:5), and even if they do bind, such antibodies may not be able to initiate the classical pathway of complement activation that leads to cell lysis.

Therefore, in view of the teachings of Janeway et al., Colman, Hogh et al., and the working example of Example 3, it appears that only peptides comprising SEQ ID NO:5 of the instant invention have the functional ability to elicit an antibody response that can lyse pathologically adherent erythrocytes in the presence of complement. As such, a skilled artisan would be unable to use the full breadth of applicant's claimed invention without conducting additional research.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 30, 32, 33, 35, 36, 38, 39, and 41 are rejected under 35 U.S.C. 102(b) as being anticipated by Shohet et al. (US Patent No. 6,191,103, see entire document).

Shohet et al. disclose multiple peptides and compositions of the band 3/anion exchange-1 protein (see entire document, particularly the abstract and Tables 1 and 2). Some of the disclosed peptides are less than 40 amino acids in length and overlap in

sequence with SEQ ID NO:5 and SEQ ID NO:6 of the instant invention (see particularly the peptides identified as 3a, 3b, and 3f in Table 2). As such, these disclosed sequences are polypeptides that consist of a fragment of SEQ ID NO:6. Further, the disclosed 3b peptide also contains positively charged lysine residues at the positions corresponding to X_2 and X_3 of SEQ ID NO:6. Shohet et al. also clearly teach that their disclosed peptide sequences can contain D amino acids (see particularly column 11, lines 5-9), and are to be used in compositions comprising pharmaceutically accepted carriers (see particularly column 16, lines 13-65).

It is noted that while base claims 30 and 36 both recite the limitation that the claimed peptides have 80% identity to SEQ ID NO:6, the length of the 80% identical region within the claimed peptide is not indicated, and base claim 36 clearly indicates that the region of 80% identity can be shorter than the entire 14 amino acids of SEQ ID NO:6 due to the recitation of fragments. The broadest reasonable interpretation of claim 30 is that members of the claimed genus need to have a region of 80% or greater identity with SEQ ID NO:6, but that this region of identity need not encompass the entire 14 amino acids of SEQ ID NO:6. As such, the 3b peptide disclosed by Shohet et al. has a region of 9 amino acids that is greater than 80% identical to a portion of SEQ ID NO:6 that is disclosed for use in compositions comprising pharmaceutically acceptable carriers and thus anticipates the claimed invention. Note that amending the claims to indicate that the claimed peptides must comprise a region that is 80% identical over the entire 14 amino acid length of SEQ ID NO:6 (thus making the claimed peptides be

between 14 and 40 amino acids in length) would obviate this rejection since fragments comprising part of the recited sequence would no longer be art.

It is also noted that Shohet et al. do not teach that administration of their peptides to a patient elicits an antibody response that is capable of specifically lysing adherent erythrocytes. However, as explained above, the peptides and compositions disclosed by Shohet et al. have the same structure as the peptides and compositions currently claimed by applicant. Given that the structure of the claimed instant invention and that of the prior art is the same, any functional property disclosed by applicant as pertaining to that structure is inherently present in the prior art structure, even if said property was not known in the prior art. "[T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." Atlas Powder Co. v. Ireco Inc., 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). See also MPEP § 2112.

Therefore, the prior art anticipates the claimed invention.

8. Claims 30, 36, 38, and 39 are rejected under 35 U.S.C. 102(b) as being anticipated by Crandall et al. (Experimental Parasitology, (1996) 82:45-53, see entire document).

Crandall et al. disclose experiments designed to map the region(s) of band 3/anion exchange-1 protein that is responsible for the increased adhesive properties seen in erythrocytes infected with *P. falciparum* (see entire document, particularly the abstract and introduction). To this end they generated a large set of overlapping decapeptides corresponding to exofacial loop 3, wherein an offset of two amino acids was used in constructing decapeptide library consisting of 25 members (see particularly the methods and materials section titled PEPSCANs, Table 1, and Figure 1). As such, Crandall et al. synthesized the 10 amino acid peptide of SEQ ID NO:3, (TFSKLIKIFQ), a particularly preferred embodiment of the invention and a specific fragment of SEQ ID NO:6 (see particularly paragraphs 39 and 40 of the instant specification). Note that this sequence contains two positively charged lysine residues at the positions corresponding to X_2 and X_3 in the sequence of SEQ ID NO:6.

Crandall et al. also disclose that a particular decamer of exofacial loop 3 (human residues 546-555) was injected into rabbits as part of a composition to elicit a polyclonal antibody response (see particularly the paragraph that spans pages 46 and 47). As has been discussed above in this office action, claim 30 does not indicate the length over which a claimed peptide and SEQ ID NO:6 must share 80% identity. The sequence of the immunizing peptide of Crandall et al. is DHPLQKTYNY, and as such the first two amino acids of this sequence are 100% identical to the last two amino acids of SEQ ID NO:5, a preferred embodiment of SEQ ID NO:6 that is the wild type sequence of human band 3/anion exchange-1 protein. Note that amending the claims to indicate that the claimed peptides and compositions contain peptides that are at least 80% identical to

SEQ ID NO:6 over the entire 14 amino acids of SEQ ID NO:6 (thus making 14 amino acids the minimum size of the claimed peptides) would obviate this rejection.

It is noted that Crandall et al. do not teach their peptides as being capable of eliciting an antibody response that lyses erythrocytes. Given that Crandall et al. teach a peptide that is a particularly preferred embodiment of the instant invention, such functional limitations are inherently present. Applicant is reminded that "the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." Atlas Powder Co. v. Ireco Inc., 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). See also MPEP § 2112.

Therefore, the prior art anticipates the claimed invention.

9. No claims are allowable.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Szperka whose telephone number is 571-272-2934. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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